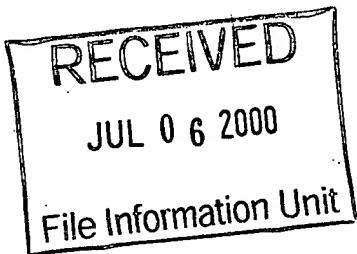


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In re Application of	
Application Number	Filed
08/186,269	1/25/95
Group Art Unit	Examiner

Paper No. #18Assistant Commissioner for Patents
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I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above-identified ABANDONED application, which is: (CHECK ONE)

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US005840299A

United States Patent [19]

Bendig et al.

[11] Patent Number: 5,840,299
[45] Date of Patent: Nov. 24, 1998

[54] HUMANIZED ANTIBODIES AGAINST LEUKOCYTE ADHESION MOLECULE VLA-4

[75] Inventors: Mary M. Bendig, London; Olivier J. Léger, Hertfordshire; José Saldanha, Enfield Middlesex; S. Tarran Jones, Radlett, all of United Kingdom; Ted A. Yednock, Fairfax, Calif.

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[21] Appl. No.: 561,521

[22] Filed: Nov. 21, 1995

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 186,269, which is a continuation-in-part of PCT/US95/01219 Jan. 25, 1995, abandoned.

[51] Int. Cl.⁶ A61K 39/395; C07K 16/28; C12P 21/08; C12N 15/13

[52] U.S. Cl. 424/133.1; 424/130.1; 424/141.1; 424/143.1; 424/144.1; 424/153.1; 424/154.1; 424/173.1; 435/7.1; 435/7.2; 435/7.21; 435/7.24; 435/69.6; 435/172.3; 435/251.3; 435/320.1; 530/387.3; 530/388.73; 530/388.75; 530/388.22; 536/23.53

[58] Field of Search 424/130.1, 133.1, 424/141.1, 143.1, 144.1, 153.1, 154.1, 173.1; 435/69.6, 172.3, 252.3, 320.1, 7.1, 7.2, 7.21, 7.24; 536/23.4, 23.5, 23.53; 530/387.1, 387.3, 388.2, 388.22, 388.7, 388.73, 388.75

[56] References Cited

U.S. PATENT DOCUMENTS

5,260,210 11/1993 Rubin et al. 435/240.23
5,530,101 6/1996 Queen et al. 530/387.3

FOREIGN PATENT DOCUMENTS

239400 9/1987 European Pat. Off. C12N 15/00
330506 8/1989 European Pat. Off. C07K 15/06
WO 90/07861 7/1990 WIPO C12P 21/00
WO 91/03252 3/1991 WIPO A61K 37/10
91/05038 4/1991 WIPO C12N 5/06
WO 93/15764 8/1993 WIPO A61K 39/395

OTHER PUBLICATIONS

Lisak et al. J. Neurol. Sciences 62: 281-293 (1983).
Teitelbaum et al. PNAS 89: 137-141 (1992).
Weiner et al. Science 259: 1321-1324 (1993).
Racke et al. J. Neuroimmunol. 46: 175-184 (1993).
Karussis et al PNAS 90: 6400-6404 (1993).

Cannella et al. Ann Neurol. 37: 424-435 (1995).
Washington et al. Ann Neurol 35: 89-97 (1994).
Dore-Duffy et al. in Frontiers in Cerebral Vascular Biology: Transport and its Regulation (eds) Dreues and Betz Plenum Press Ny 1993 pp. 243-248.
Monshizadegan et al., "VLA-4-dependent adhesion activities of U937 cells and guinea pig bronchoalveolar lavage leukocytes", 1993, *Agents Actions* 39, pp. C177-C179.
Kettleborough et al., "Humanization of a mouse monoclonal antibody by CDR-grafting the importance of framework residues on loop conformation", 1991, *Protein Engineering*, vol. 4, No. 7, pp. 773-783.

Yednock et al. "Prevention of experimental autoimmune encephalomyelitis by antibodies against $\alpha 4\beta 1$ integrin", 1991, *Letters to Nature*, vol. 356, pp. 63-66.

W. J. Harris and S. Emery, "Therapeutic antibodies—the coming of age", 1993, *Tibtech*, vol. 11, pp. 42-45.

S. C. Emery and J. R. Adair, "Humanised monoclonal antibodies for therapeutic applications", 1994, *Exp. Opin. Invest. Drugs*, vol. 3, pp. 241-251.

S. M. Edgington, "How Sweet It Is: Selectin-Mediating Drugs", 1992, *Bio/Technology*, vol. 10, pp. 383-389.

Elices et al., "VCAM-1 on Activated Endothelium Interacts with the Leukocyte Integrin VLA-4 at a Site Distinct from the VLA-4/Fibronectin Binding Site", 1990, *Cell*, vol. 60, pp. 577-584.

Dijkstra et al., "Multiple sclerosis: some possible therapeutic opportunities", 1993, *Tips Reviews*, vol. 14, pp. 124-129.

A. Mountain and J.R. Adair, "Engineering Antibodies for Therapy", 1992, *Biotech Genetic Engineering Reviews*, vol. 10, pp. 10-13.

P.A. Ward and M.S. Mulligan, "Blocking of adhesion molecules in vivo as anti-inflammatory therapy", 1994, *Therapeutic Immunol*, vol. 10, pp. 165-171.

L. K. Jolliffe, "Humanized Antibodies: Enhancing Therapeutic Utility Through Antibody Engineering", 1993, *Intern Rev Immunol*, vol. 10, pp. 241-250.

Albelda Faseb J. 8: 504-512 (1994).

Kahan Curr Opin Immunology 4: 553-560 (1992).

Natanson et al. Ann Intern Med: 120: 771-783 (1994).

Dalakas Ann. Neurol. 37(51): 52-513 (1995).

Paul (ed) Fundamental Immunology Raven Press NY 1993 p. 242 only.

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[57] ABSTRACT

The invention provides humanized immunoglobulins that specifically bind to the VLA-4 ligand, and methods of treatment using the same. The methods are particularly useful for treatment of multiple sclerosis.

29 Claims, 16 Drawing Sheets